REMARKS

Claims 1-13 and 22-25 were pending. Claims 1 and 13 have been amended. Claims 27-29 are added. Claims 2, 8-12, and 14-21 are canceled. No new matter is added.

Claims 1 and 3-7 have been rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. The Office Action states that the application lacks description for any method of activating oxidative phosphorylation in an *in vitro* synthesis method.

Without conceding to the correctness of the rejection, Applicants have amended Claim 1 to recite the use of a bacterial cell extract in the absence of polyethylene glycol and presence of magnesium at a concentration from about 5 mM to about 20 mM. Applicants respectfully submit that the present Claims provide sufficient guidelines for one of skill in the art to practice the claimed methods.

In view of the above amendments and remarks, withdrawal of the rejection is requested.

Claims 13 and 22, and 24-26 have been rejected as anticipated by Baranov *et al.* (1993) Methods in Enzymology 217, 123-142 and Chen *et al.* (Methods in Enzymology 101:674-690). The Office Action states that Baranov *et al.* teach a method of synthesizing biological macromolecules in a reaction mix comprising an extract from *E. coli* grown in glucose containing medium, comprising magnesium at a concentration of from about 5 mM to 20 mM, and substantially free of polyethylene glycol. The *E coli* extract of Baranov is stated to be prepared using a standard method such as that taught by Chen *et al.* Claim 23 is rejected under 35 U.S.C. 103(a) as unpatentable over Baranov *et al.* and Chen *et al.*

Applicants respectfully submit that the presently claimed invention is not anticipated by the cited art. Claim 1 has been amended to recite that spermine or spermidine are present at a concentration of at least 1 mM. As shown in the cited Baranov Table 1, example 5, spermidine was provided only at a very low concentration. At 0.05 mM, the spermidine was present at a concentration far lower than that of the present claims. Therefore, the invention of Claim 13 is distinguished from the methods of the cited art.

Claim 13 has further been amended to recite that oxidative phosphorylation is activated in the reaction mixture and that a high energy phosphate source is not provided, and new dependent claims 27 and 28 have been added, which speak to the ability of the methods of the invention to accomplish synthesis in the absence of secondary energy sources, including a high

energy phosphate source. As described by Applicants in the previous response, the present invention is based on the extraordinary discovery that reaction conditions for cell-free synthesis can be manipulated in such a way as to provide for oxidative phosphorylation, as evidenced by the significant synthesis of polypeptides even in the absence of an exogenous energy source. The ability to activate oxidative phosphorylation could not have been predicted by one of skill in the art, and could not have been predicted to arise from the combination of reaction conditions set forth by Applicants.

In view of the above amendments and remarks, Applicants respectfully submit that the presently claimed invention is not taught or suggested by the cited reference. Withdrawal of the rejections is requested.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number STAN-273.

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Respectfully submitted,
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